176. A method of production according to Claim 94 wherein said host cell is *E. coli*.

177. A method for the production of glial cell line-derived neurotrophic factor polypeptide, comprising the steps of:

(a) culturing a host cell transformed or transfected with a vector according to claim 137 under conditions suitable for the expression of glial cell line-derived neurotrophic factor polypeptide; and optionally

(b) isolating said glial cell line-derived neurotrophic factor polypeptide expressed by said host cell.--

No new matter has been added with the addition of these claims. Please cancel claim 93.

REMARKS

Claims 88-94 and 117-158 are pending in the application. Claims 88-94, 118-120, 135, 150 and 152-157 have been allowed.

As described above, the specification has been amended so that the figures are more clearly referenced by the appropriate sequence identification numbers. With reference to the sequences:

- the nucleic acid and amino acid sequences depicted in Figure 13 correspond to those shown in SEQ ID NO:3 and SEQ ID NO:4, respectively
- the nucleic acid and amino acid sequences depicted in Figure 19 correspond to those shown in SEQ ID NO:5 and SEQ ID NO:6, respectively.

The claims have been amended to provide a more consistent use of the term "polypeptide" throughout the claims. In the course of prosecution, amended claims had used the terms glial cell line-derived neurotrophic factor, factor, polypeptide and glial cell line-derived neurotrophic factor polypeptide, each to refer to the subject matter of the invention. The amendments provide one term, "glial cell line-derived neurotrophic factor polypeptide", to more clearly refer to those protein products particularly identified and described in the

claims by the specified nucleic acid and amino acid sequences. The claims were also amended to refer to these protein products' capability to promote dopamine uptake by dopaminergic neurons. Thus, the claimed subject matter does not rely on the name "glial cell line-derived neurotrophic factor" to identify the protein products, but rather on the particularly claimed structural and biological characteristics which clearly distinguish the protein products from other materials.

Allowed claim 88 was amended to use terminology (i.e., "purified and isolated") that is consistent with that of the remaining claims (e.g., allowed claims 118-120). In accordance with its common usage in biotechnology, the phrase "purified and isolated nucleic acid sequence" is used in the present application and claims to refer to nucleotide sequences which are not in a naturally occurring form.

Allowed claims 94, 135 and 150 were amended to use terminology (i.e., "transformed or transfected") that is consistent with that of the remaining claims (e.g., claim 127). Amendments also clarify that expression of a GDNF-encoding nucleic acid is aided by operative linkage to an expression regulatory element (e.g., non-native promoter). Such a non-native promoter is exemplified by the SV40 and tac promoters as described in Examples 5 and 6.

Claims 159-161 were added to provide the subject matter of claim 135 in independent claim form. Claims 162-164 were added to further provide for the preferred percent identity alternatives as described in the specification on page 20, lines 11-12.

Allowed claims 152 and 153, previously dependent on allowed claim 150, were amended to place the claimed subject matter in independent claim form. Claim 165 was added to place the aspect of claim 150 (a)(i) in independent claim form. Claims 166-174 were added to provide dependent claims to 152, 153 and 165. These dependent claims correspond to previously allowed claims 154-157 which depend from claim 150.

Claims 175 and 176 were added to specify *E. coli* production with respect to allowed claims 88 and 94. Claim 177 was added due to the amendment of claim 149 wherein the reference to claim 137 was deleted to remove the multiple dependency of claim 149.

No new matter has been added with these amendments or newly added claims.

Section 112, First Paragraph Rejections

The Examiner rejected claims 122 and 151 which describe the inclusion of an amino terminal residue. The Examiner stated that no basis for the amino terminal residue had been pointed to in the specification. Applicants respectfully traverse the rejection and direct the Examiner's attention to page 19, lines 33-35, where the expression of GDNF proteins having an amino-terminal methionine residue is first described. In addition, it is well-known in the art that the use of recombinant bacterial expression systems, as described in Example 6 (page 77) results in the addition of a methionine residue to the expressed protein.

The Examiner rejected claim 124 which describes the inclusion of nucleotides encoding a pre-pro amino acid sequence. The Examiner states that it does not appear that the pre-pro sequences are identical for the rat and human mature GDNF sequences. The claim, however, depends from allowed claims 118 and 119 both of which describe human GDNF nucleotide and amino acid sequences. Thus, Applicants respectfully submit that this rejection may properly be withdrawn.

Claim 136 has been amended to recite the terminology of "in excess of 90% identical" as provided in the Specification at page 20, line 12, to describe one particularly preferred degree of homology or percent identity. Thus, the rejection of this claim and dependent claims 137-142 may properly be withdrawn.

Claims 117, 121 and 125 have been amended to remove the reference to "reduced stringency". The claims now recite that the hybridizing conditions must comprise certain specifically required conditions as are set forth in the Examples, such as Example 2. Thus, Applicants respectfully submit that the rejection of these claims, as well as those claims which depend therefrom, may properly be withdrawn.

Section 112, Second Paragraph Rejections

In order to particularly point out and distinctly claim the subject matter of the invention, claims 117, 121 and 125 have also been amended to remove the recitation of "wherein said condition include" which was considered unclear by the Examiner. The claims

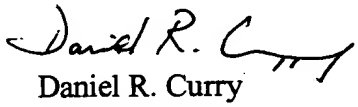
now recite particular hybridizing conditions as are set forth in the Examples. Thus, Applicants respectfully submit that the rejection may properly be withdrawn.

Claims 124 and 125 were amended to refer to SEQ ID NO:26 which has been added by amendment to separately depict the amino acid sequence illustrated in SEQ ID NO:25.

The amendments should not be construed as an acquiescence to the rejections and have been made solely to expedite the prosecution of this application. Applicants reserve the right to pursue the previous claims in another application(s).

For the foregoing reasons and in view of the amendments, Applicants respectfully request reconsideration of and withdrawal of the outstanding rejections. Applicants' representative would appreciate the opportunity to talk with the Examiner, in person or by telephone, to discuss any remaining questions and facilitate the prosecution and allowance of the application or to place the case in better form for appeal.

Respectfully submitted,



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